II. Remarks

A. Status of the Claims

Claims 1, 3, 8-10, 12-27, 29-32, and 35-47 are currently pending.

B. Claim Rejection Under 35 U.S.C. § 103(a)

Claims 1, 3, 8-10, 12-27, 29-32, and 35-47 were rejected under 35 U.S.C. § 103(a) over the combination of Nutt et al. (Clinical Pharmacology and Therapeutics, Vol. 15, Number 2, pp. 156-166) ("the Nutt article"), Mayer et al. (U.S. 5,556,838)("the Mayer patent"), Ockert (U.S. 5,376,662) ("the Ockert patent"), and European Patent No. 0 193 355 ("the Hynes patent"). In the Advisory Action, the Examiner states:

> Applicant in his arguments alleges criticality to the specific ratios of the claimed components. However, the claims are not dwarn [sic] to any specific ratios. Applicant in the claims uses functional language in order to define the claimed ratios.

The Advisory Action, page 2.

The rejection is respectfully traversed.

The Manual of Patent Examining Procedure states that "[t]here is nothing inherently wrong with defining some part of an invention in functional terms," and that "[a] functional limitation **must be evaluated and considered**, just like any other limitation of the claim, for what it fairly conveys to a person of ordinary skill in the pertinent art in the context in which it is used." MPEP, section 2173.05(g) (emphasis added).

Present independent claims 1 and 41 define the ratios of the opioid antagonist to the opioid agonist to the acetaminophen in the claimed dosage forms by using functional terms. Claims 1 and 41 recite that the ratios of the opioid antagonist to the opioid agonist to the acetaminophen are such that

(i) the combination is analgesically effective when it is administered orally,

(ii) it is aversive in physically dependent human subjects when administered orally; and

(iii) it maintains an analgesic effect but does not increase analgesic efficacy of the opioid agonist together with the acetaminophen, relative to when the opioid agonist and the acetaminophen are administered orally without said opioid antagonist.

Functional language is permissible and "**must be evaluated and considered**, just like any other limitation of the claim," in accordance with section 2173.05(g) of the Manual of Patent Examining Procedure. (emphasis added).

The combination of the cited references does not teach or suggest the ratios recited in claims 1 and 41, and does not provide any suggestion or motivation to combine an opioid agonist, an opioid antagonist and acetaminophen in the ratios recited in present claims 1 and 41. On page 2 of the final Office Action mailed on July 7, 2010, the Examiner states that the rejection is "for the reasons set forth on pages 2-5 of the office action of May 26, 2009." However, the rejection in the Office Action of May 26, 2009, has been overcome by the arguments presented in the response filed on November 23, 2009.

As stated in the response filed on November 23, 2009, the combination of the cited references does not provide a reason to the skilled person to combine the individual

components of the cited references in the manner suggested by the Examiner and to formulate a dosage form as recited in claims 1 and 41. Moreover, even if the references were properly combinable (a position which is vehemently denied by the Applicants), the combination of the cited references would still not render claims 1 and 41 obvious, because the combination of the cited references fails teach or suggest the ratios recited in claims 1 and 41.

In response to the Examiner's statement on page 3 of the Office Action of May 26, 2009, that "[t]he primary reference teaches that the mixture has significantly less miotic, behavioral and subjective effect than methadone alone," Applicants note that the portion of the Nutt article believed to be relied upon by the Examiner states:

> **By the parenteral route**, the mixtures have significantly less miotic, behavioral, and subjective effects than methadone alone ...

Nutt, Abstract (emphasis added).

Applicants respectfully submit that the statement on page 165, right column, first full paragraph, of the Nutt article that "... by the oral route ...[the methadone-naloxone mixture described therein] ... is **indistinguishable** from methadone alone" (emphasis added) (alone or in combination with the cited references) would not have motivated the skilled person to formulate an oral dosage form which "is **aversive** in physically dependent human subjects when administered **orally**," as recited in independent claims 1 and 41.

In response to the Examiner's reliance on the Mayer patent, Applicants note that the Mayer patent is directed in part to "a method of **alleviating** withdrawal symptoms in a mammal" (column 2, lines 23-33). The Mayer patent states, e.g., that naloxone (an opioid antagonist) produces withdrawal symptoms (column 7, lines 23-26). Applicants therefore submit that the Mayer patent (alone or in combination with the cited references)

would not have motivated the skilled person to formulate an oral dosage form comprising "an opioid antagonist, and which "is aversive in physically dependent human subjects when administered orally" as recited in independent claims 1 and 41.

In response to the Examiner's reliance on the Ockert patent, Applicants note that the Ockert patent is directed in part to "local administration of naloxone at or near the nerve trauma site." The Ockert patent, column 2 lines 35-48. The Ockert patent states, e.g., that "[n]aloxone and other opiate-antagonists competitively **antagonize** both exogenous opiates (such as heroine or morphine) and endogenous opioids (such as B-endorphin, enkephalins, and dynorphin at both peripheral and central nerve opiate receptors)." The Ockert patent, column 4, lines 8-12. Applicants therefore submit that the Ockert patent (alone or in combination with the cited references) would not have motivated the skilled person to combine an opioid agonist and an opioid antagonist in a dosage form which "is aversive in physically dependent human subjects when administered orally" as recited in independent claims 1 and 41.

For the foregoing reasons, Applicants submit that a dosage form comprising the combination of an opioid agonist, acetaminophen and an opioid antagonist recited in independent claims 1 and 41 would not have been obvious in view of the combination of the cited references.

With further regard to claims 46 and 47, Applicants submit that the combination of the cited references would not have taught or suggested a dosage form "consisting of the opioid agonist, the acetaminophen, the opioid antagonist, and one or more pharmaceutically acceptable inert excipients" as recited in these claims. This is because fluoxetine, norfluoxetene or salts thereof of the Hynes patent and the NMDA receptor blockers of the Mayer patent are excluded from such dosage form by virtue of the "consisting of" language.

Reconsideration and withdrawal of the rejection is respectfully requested.

C. Double Patenting

Claims 1, 3, 8-10, 12-27, 29-32, and 35-47 were rejected on the ground of nonstatutory obviousness-type double patenting over claims 1-27 of U.S. Patent No. 7,419,686 in view of European Patent Application No. 0 13 355.

Claims 1, 3, 8-10, 12-27, 29-32, and 35-47 were rejected on the ground of nonstatutory obviousness-type double patenting over claims 1-21 of U.S. Patent No. 7,172,767 in view of European Patent Application No. 0 13 355.

Claims 1, 3, 8-10, 12-27, 29-32, and 35-47 were rejected on the ground of nonstatutory obviousness-type double patenting over claims 1-29 and 59-63 of U.S. Patent No. 6,696,066 in view of European Patent Application No. 0 13 355.

Claims 1, 3, 8-10, 12-27, 29-32, and 35-47 were rejected on the ground of nonstatutory obviousness-type double patenting over claims 1-23 of U.S. Patent No. 6,475,494 in view of European Patent Application No. 0 13 355.

Claims 1, 3, 8-10, 12-27, 29-32, and 35-47 were rejected on the ground of nonstatutory obviousness-type double patenting over claims 1-25 and 50 of U.S. Patent No. 6,277,384 in view of European Patent Application No. 0 13 355.

Claims 1, 3, 8-10, 12-27, 29-32, and 35-47 were rejected on the ground of nonstatutory obviousness-type double patenting over claims 1-21 of U.S. Patent No. 6,375,957 in view of European Patent Application No. 0 13 355.

Applicants acknowledge these double patenting rejections, but respectfully request that the requirement to file terminal disclaimers to obviate these rejections be held in abeyance until such time as claims are otherwise held to be allowable.

III. Conclusion

An early and favorable action on the merits is earnestly solicited. According to currently recommended Patent Office policy, the Examiner is specifically authorized to contact the undersigned by telephone in the event that a telephonic interview will advance the prosecution of this application.

Respectfully submitted,
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